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8-27-97
Date

Alexandra M. Parsons
Alexandra M. Parsons

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Lynn E. Spitzer et al.

Serial No.: 08/288,057

Filing Date: 10 August 1994

For: PROSTATIC CANCER VACCINE

Examiner: P. Gambel

Group Art Unit: 1816

DECLARATION OF LYNN E. SPITLER, M.D.
PURSUANT TO 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Lynn E. Spitzer, declare as follows:

1. I am a coinventor of the subject matter in the above-referenced application. I have been a practicing immunologist for many years. A copy of my *curriculum vitae* is attached hereto as Exhibit A.

2. I have been managing clinical trials of OncoVaxTM prostate cancer vaccine which is recombinant human prostate specific antigen (rhPSA) formulated in liposomes with lipid A as adjuvant. Lipid A is a preferred adjuvant because of its ability to stimulate cell-mediated immunity in general and production of cytotoxic T cells (CTL) in particular, as opposed to alum which enhances the antibody response.

3. We conducted four clinical Phase I/II trials with 4 or 5 patients in each trial. In the first two trials, eligible patients had surgically incurable and hormone-resistant prostate cancer as

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well as intact immune responses as measured by ability to respond to recall antigens. Patients were given 1 ml of the vaccine containing 100 ^{PSA 25} µg rHPLS and 200 µg lipid A. In the first trial, the vaccine was administered intramuscularly in two divided doses on two extremities with intact regional lymph nodes every 30 days times 3. In this trial, one patient showed skin test sensitivity to PSA with a diameter of erythema of 18 mm, and a diameter of induration of 10 mm (when diameters of more than 5 mm are considered positive responses).

4. In the second trial, the same dosage and regimen was used except that an intravenous route was employed. Again, one of five patients showed reactivity to a skin test with PSA with a diameter of erythema of 10 mm.

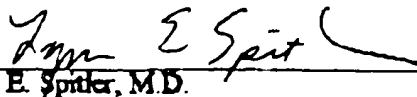
5. In a third trial, the adjuvant GM-CSF was added to the protocol and the vaccine was administered with the same protocol intramuscularly. In this test, all ^{4 evaluable 25} 8 patients showed skin test reactivity to PSA with a mean diameter of erythema of 37 mm. One patient had an erythema diameter of 70x50 mm.

6. In the fourth trial, patients were treated with cyclophosphamide to diminish suppressor cell activity and the vaccine was administered intracutaneously with the addition of *Bacillus Calmette-Guerin* (BCG) at the site of vaccine administration. In this trial, 4 of the 5 patients showed a skin response to PSA with a mean diameter of erythema of 17 mm and a mean induration diameter of 9 mm.

7. The data are shown in detail on attached Exhibit B. These results show that administration of Onco VaxTM is successful in eliciting a cellular response in these patients, especially in the presence of a suitable adjuvant.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Executed at Tiburon, California on 26 August 1997, by


Lynn E. Spitzer, M.D.

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Serial No. 08/288,057
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** TOTAL PAGE.08 **

CURRICULUM VITAE

LYNN E. SPITLER, M.D.

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Social Security #366-38-1697

Education:

University of Michigan, Ann Arbor, Michigan	1956-1959
University of Michigan Medical School Ann Arbor, Michigan M.D. (cum laude)	1959-1963

Training:

Intern	Highland Alameda County Hospital Oakland, California	1963-1964
Resident	University of California School of Medicine San Francisco, California	1964-1966
Research Fellow	H.S. Lawrence, M.D. Department of Medicine - Immunology New York University New York, New York	1966-1967
Immunology Trainee	H. Hugh Fudenberg, M.D. University of California School of Medicine San Francisco, California	1967-1969

Teaching Appointments and Employment:

Instructor of Medicine in Residence University of California School of Medicine San Francisco, California 94143	1970-1971
Assistant Professor of Medicine in Residence University of California School of Medicine San Francisco, California 94143	1971-present
Research Associate Cancer Research Institute University of California School of Medicine San Francisco, CA 94143	1971-1978
Director, Melanoma Center Northern California Health Center San Francisco, California 94118	1978-1990
Director of Research Children's Hospital of San Francisco San Francisco, California 94118	1978-1981
Member, Graduate Group in Comparative Pathology Department of Comparative Pathology University of California, Davis Davis, California	1976-1981
Senior Vice President XOMA Corporation 2910 Seventh Street Berkeley, California 94710	1981-1988
Associate Scientific Director Biotherapeutics, Inc. 357 Riverside Drive Franklin, Tennessee, 37065-1676	1988-1989

Director Northern California Melanoma Centers 1895 Mountain View Drive Tiburon, California 94920	1990-present
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President Jenner Technologies 1895 Mountain View Drive Tiburon, California 94920	1991-present
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Awards and Honors:

Recipient: Dernham Senior Fellowship California Div. of the American Cancer Society	1969-1971
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Recipient: Research Career Development Award National Institutes of Health	1971-1976
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Alpha Omega Alpha (Junior year)	1961
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Outstanding Young Women of America	1968
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Who's Who of American Women	1972
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Who's Who in the West	1973
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Board Certification:

American Board of Internal Medicine	1972
American Board of Allergy and Immunology	1974

Licensure:

Michigan	25985
New York	96454
California	C-26446

Memberships in Professional Societies:

American Association of Immunologists
American Association for the Advancement of Science
Alpha Epsilon Iota
Western Society for Clinical Research
American Federation of Clinical Research
Society of Biological Therapy
American Association for Cancer Research

Patents:

Patent #4,489,810 for "Composition and Method for Transplantation Therapy"
Patent #4,590,071 for "Human Melanoma Specific Immunotoxins"

PUBLIC SERVICE

National Review Committees:

Allergy and Immunology Research Committee, NIAID, NIH	1976-1980
Merit Review Board in Immunology, VA, Washington, D.C. (Chairman 1979-1980)	1976-1980

Editorial Boards:

The Journal of Immunology	1975-1978
The International Journal of Immunopharmacology	1979-1984
Immunologia Clinica e Sperimentale	1982-1986
Antibody Immunoconjugates and Radiopharmaceuticals (Associate Editor)	1987-present
Molecular Biotherapy	1987-present
Cancer Biotherapy	1991-present

Manuscript Reviews:

American Review of Respiratory Disease
Annals of Allergy
Annals of Internal Medicine
Archives of Dermatology
Archives of Internal Medicine
California Medicine
Cancer
Cancer Immunology and Immunopathology
Cancer Research
Cellular Immunology
Chest
Infection and Immunity
Infectious Disease and Immunology
International Journal of Immunopharmacology
Journal of Clinical Investigation
Journal of Immunology
Journal of Infectious Diseases
Journal of the American Academy of Dermatology
Molecular Biotherapy
Nature
New England Journal of Medicine
Science
The Western Journal of Medicine

Special Consulting:

National Institutes of Health Grant Reviews
National Institutes of Health Site Visits
United States Tuberculosis Panel Task Group
Atomic Energy Commission Site Visits
Public Education Panel, National Multiple Sclerosis Society
Review of Grant Applications for the National Science Foundation
Enterprise for High School Students, Medical Apprenticeship Program,
San Francisco, California
Board of Directors, San Francisco Unit, American Cancer Society
Research and Human Experimentation Committee, Children's Hospital
of San Francisco
U.S. Energy Research Development Administration Site Visits

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3. Cochrum K.D., Spitler L.E., Najarian J.S., and Fudenberg H.H.: A new source of large numbers of lymphocytes and studies on their culture. In Proceedings of the Third Annual Leukocyte Culture Conference. Edited by W.O. Rieke, Appleton-Century-Crofts, New York, New York, 1969, pp. 169-175.
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8. Levin A.S., Spitler L.E., Stites D.P., and Fudenberg H.H.: Wiskott- Aldrich syndrome: a genetically determined cellular immunological deficiency. Clinical and laboratory responses to therapy with transfer factor. Proc. Natl. Acad. Sci. 67:821-827, 1970.
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Revised January, 1992

Gamma Interferon production after peptide stimulation of lymphocytes

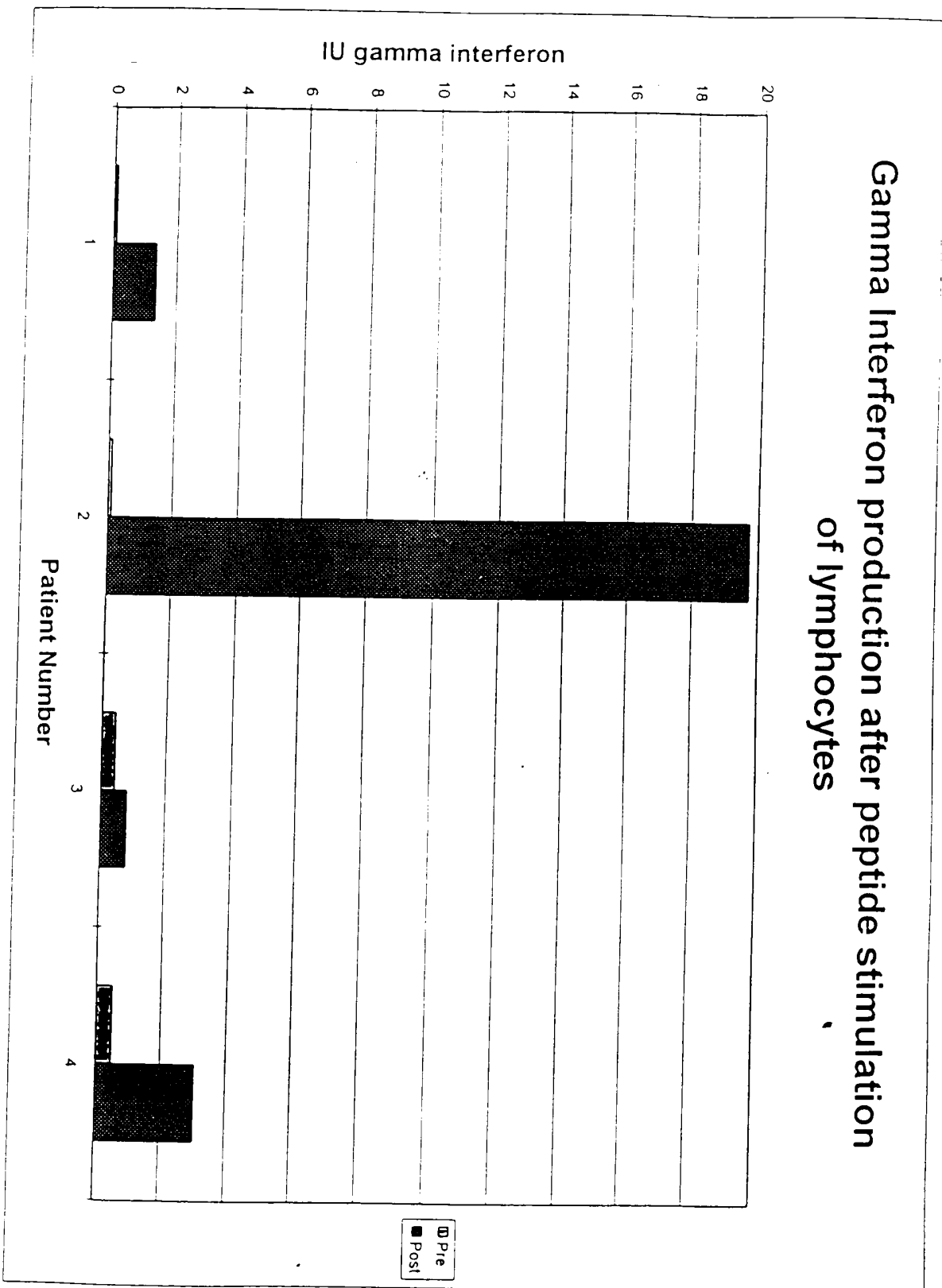


Exhibit B

IL-4 production after peptide stimulation of lymphocytes

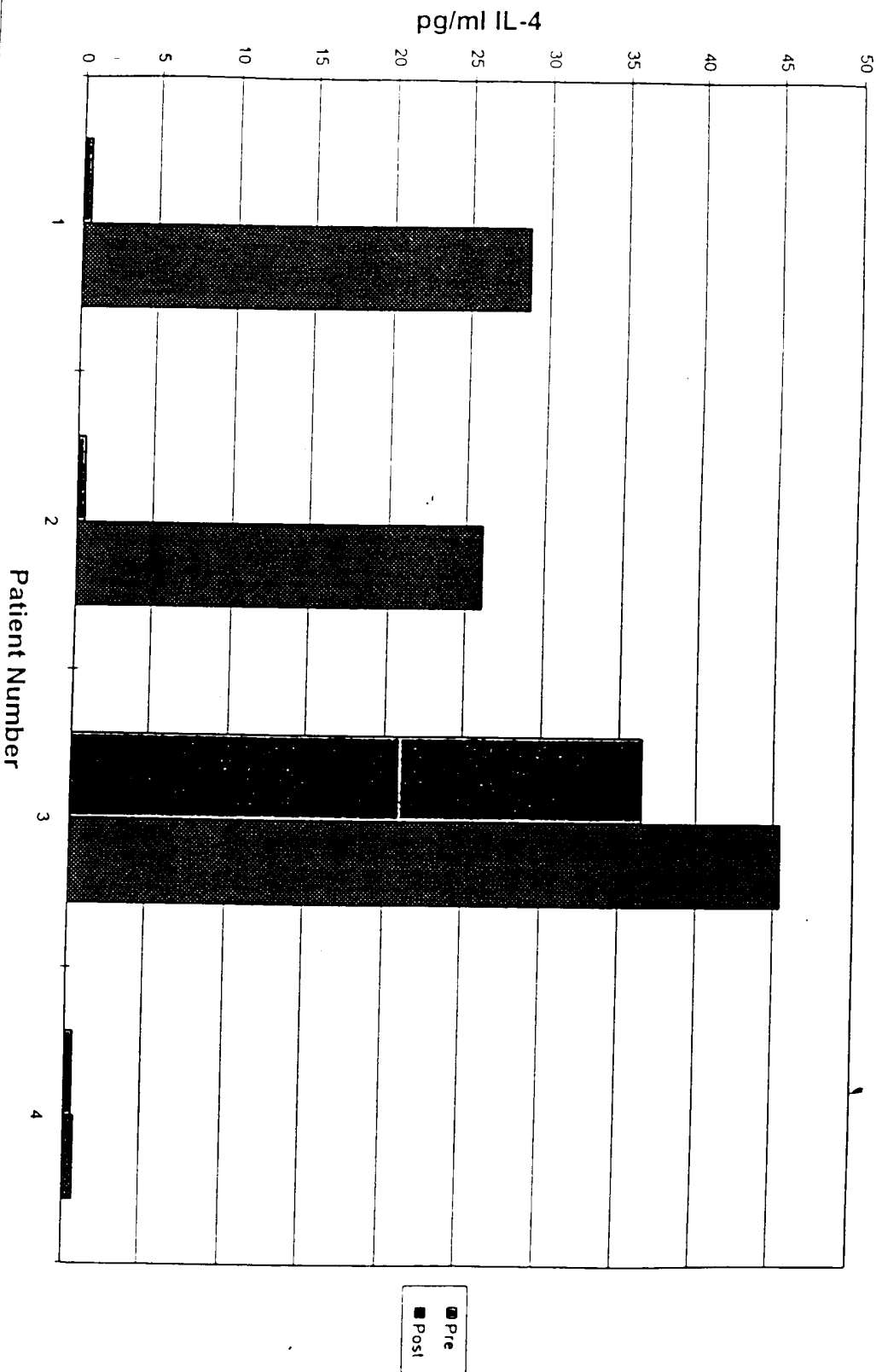


Exhibit B

Prostate Cancer Vaccine Trials Day 90 Skin Test Results

Clinical Trial #1 – Immunization of Patients with Prostate Cancer with OncoVax-P™ (Prostate Cancer Vaccine)

	PSA		Buffer		CEA	
	Erythema	Induration	Erythema	Induration	Erythema	Induration
001 AW	2x2	0	0	0		
002 JH	ND	ND	ND	ND		
003 MD	18x18	10x10				
004 MED	0	0	0	0		
005 HN	0	0	0	0		
006 JLB	0	0	0	0		

Clinical Trial #2 – Intravenous Immunization of Patients with Prostate Cancer with OncoVax-P™ (Prostate Cancer Vaccine)

	PSA		Buffer		CEA	
	Erythema	Induration	Erythema	Induration	Erythema	Induration
101 RT	0	0	0	0		
102 ER	0	0	0	0		
103 MC	0	0	0	0		
104 TM	0	0	0	0		
105 AF	ND	ND	ND	ND		
106 WC	10X10	0	0	0		

Clinical Trial #3 – Immunization of Patients with Prostate Cancer with OncoVax-P™ (Prostate Cancer Vaccine) with GM-CSF

	PSA		Buffer		CEA	
	Erythema	Induration	Erythema	Induration	Erythema	Induration
201 AM	30x20	0			0	0
202 ASP	35x30	30x30			7x7	7x7
203 CN	70x50	0			0	0
204 JA	ND	ND			ND	ND
205 GS	37x22	0			0	0

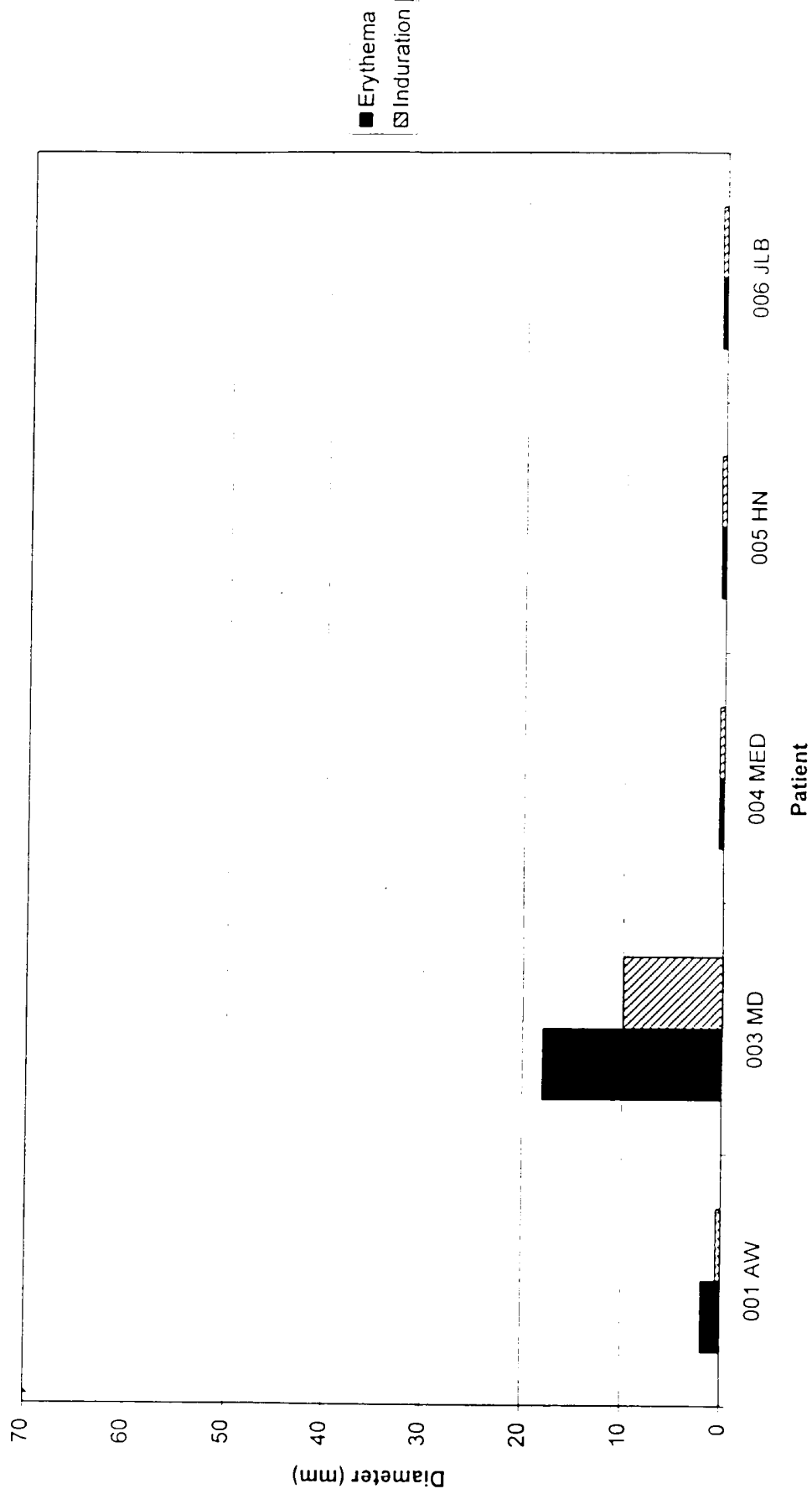
Clinical Trial #4 – Immunization of Patients with Prostate Cancer with OncoVax-P™ (Prostate Cancer Vaccine with BCG)

	PSA		Buffer		CEA	
	Erythema	Induration	Erythema	Induration	Erythema	Induration
301 GS	32x28	32x28			0	0
302 AR	15x15	15x15			0	0
303 JE	15x12	0			0	0
304 ML	0	0			0	0
305 RD	30x30	0			0	0

ND = Not Done

Exhibit B
Spitler

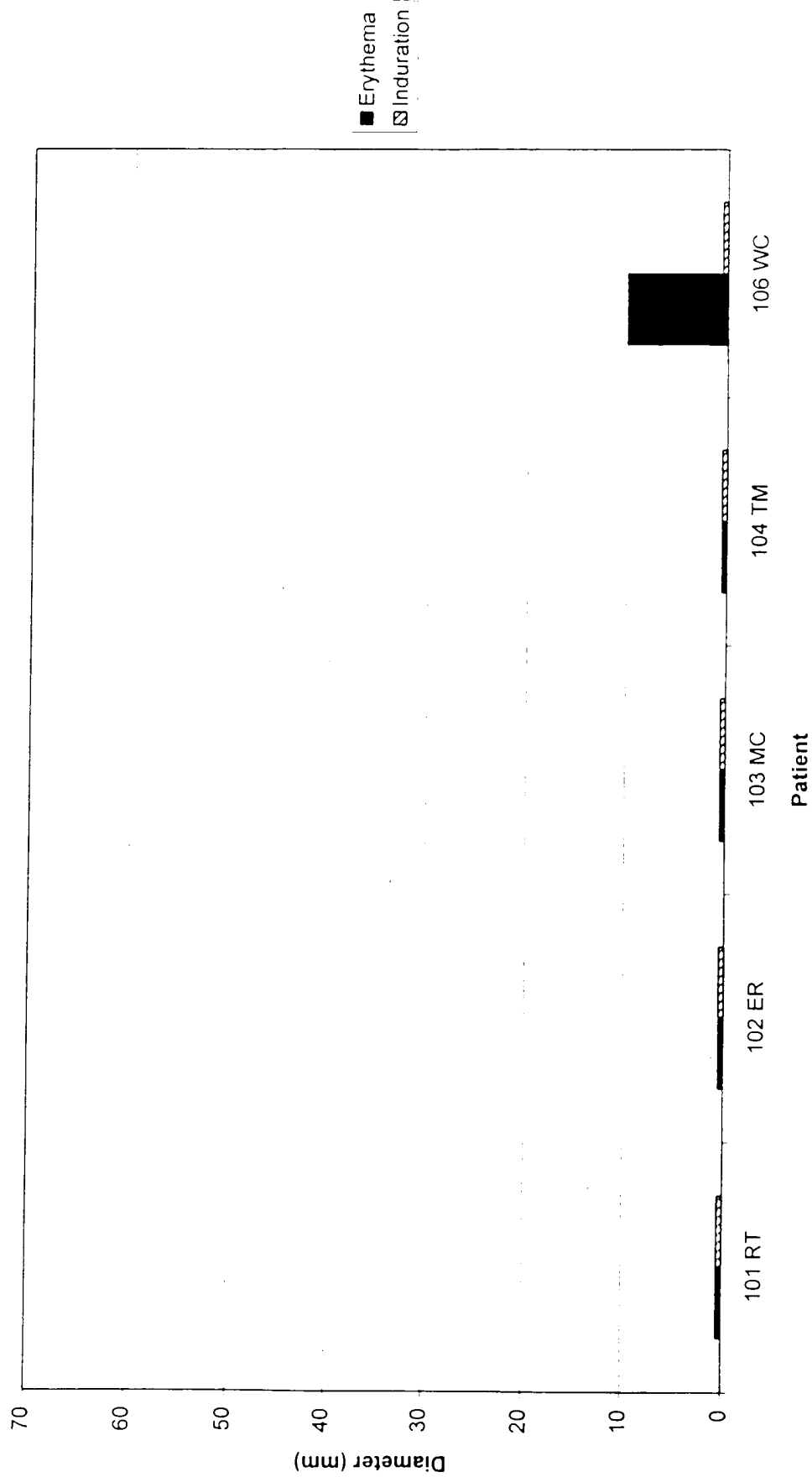
Skin Test Reactivity to PSA
Clinical Trial #1
Immunization of Patients with Prostate Cancer with OncoVax-P™



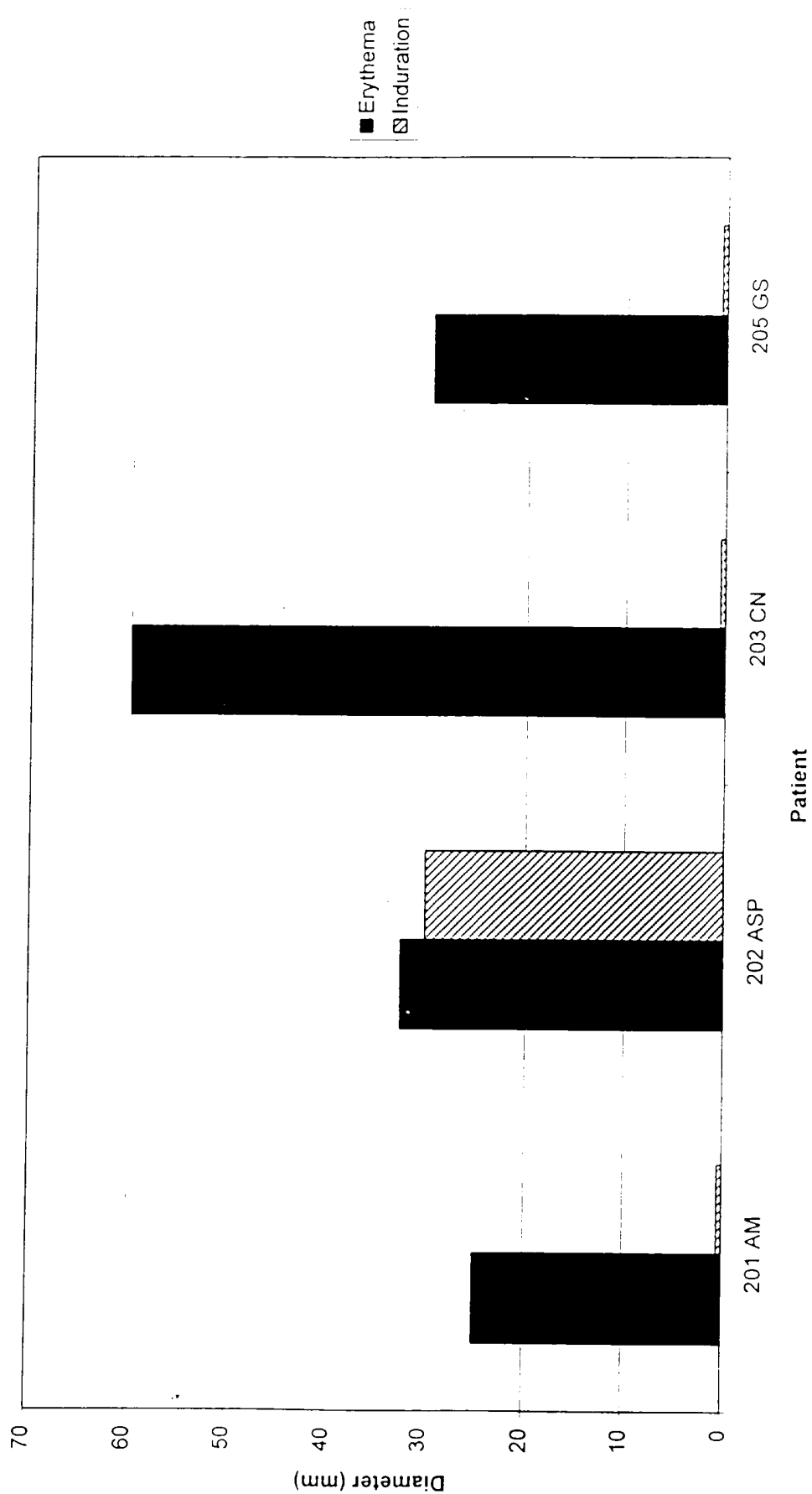
Skin Test Reactivity to PSA

Clinical Trial #2

Intravenous Immunization of Patients with Prostate Cancer with OncoVax-P™



Skin Test Reactivity to PSA
Clinical Trial #3
Immunization of Patients with Prostate Cancer with OncoVax-P™ with GM-CSF



Skin Test Reactivity to PSA
Clinical Trial #4
Intravenous Immunization of Patients with Prostate Cancer with OncoVax-P™ with BCG

